10/540,075

```
=> d his ful

     (FILE 'REGISTRY' ENTERED AT 17:08:17 ON 13 MAR 2007)
L1             STR
L6          2120 SEA SSS FUL L1
L10            STR
L11            1 SEA SSS SAM L10
L12           29 SEA SUB=L6 SSS FUL L10

     FILE 'HCAPLUS' ENTERED AT 17:51:31 ON 13 MAR 2007
L13            2 SEA ABB=ON  PLU=ON  L12
                 D STAT QUE L13
                 D IBIB ABS HITSTR L13 1-2
L14            6 SEA ABB=ON  PLU=ON  "ROTTLANDER MARIO"/AU
L15           23 SEA ABB=ON  PLU=ON  ("RITZEN A"/AU OR "RITZEN ANDREAS"/AU)
L16            8 SEA ABB=ON  PLU=ON  "NORGAARD M"/AU OR ("NORGAARD MORTEN"/AU
                 OR "NORGAARD MORTEN BANG"/AU)
L17            6 SEA ABB=ON  PLU=ON  "KHANZHIN NIKOLAY"/AU
L18           14 SEA ABB=ON  PLU=ON  ("TORNOE C"/AU OR "TORNOE C W"/AU) OR
                 ("TORNOE CHRISTIAN"/AU OR "TORNOE CHRISTIAN W"/AU)
L19           53 SEA ABB=ON  PLU=ON  L14 OR L15 OR L16 OR L17 OR L18
L20           52 SEA ABB=ON  PLU=ON  L19 NOT L13
                 D STAT QUE L20
                 D IBIB ABS HITSTR L20 1-52

     FILE HCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     the American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 13 Mar 2007  VOL 146 ISS 12
     FILE LAST UPDATED: 12 Mar 2007  (20070312/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

      This file contains CAS Registry Numbers for easy and accurate
      substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   12 MAR 2007  HIGHEST RN 926069-79-6
     DICTIONARY FILE UPDATES:  12 MAR 2007  HIGHEST RN 926069-79-6

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.
```

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE BEILSTEIN
FILE LAST UPDATED ON JANUARY 10, 2007

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,780,003 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

```
************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.      *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.              *
* FOR PRICE INFORMATION SEE HELP COST                      *
************************************************************
```

NEW
* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.
* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.

=>
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:51:31 ON 13 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

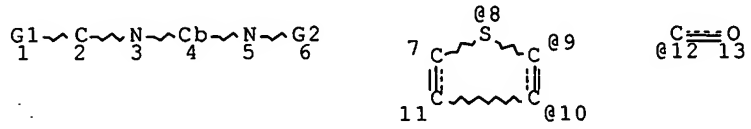
FILE COVERS 1907 - 13 Mar 2007 VOL 146 ISS 12
FILE LAST UPDATED: 12 Mar 2007 (20070312/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=>

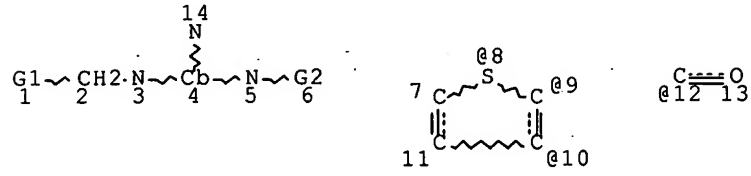
=> d stat que l13
L1   STR



VAR G1=8/9/10
VAR G2=12/SO2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
L6   2120 SEA FILE=REGISTRY SSS FUL L1
L10   STR



VAR G1=8/9/10
VAR G2=12/SO2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY AT   4
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   7
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L12   29 SEA FILE=REGISTRY SUB=L6 SSS FUL L10
L13   2 SEA FILE=HCAPLUS ABB=ON PLU=ON L12

=>

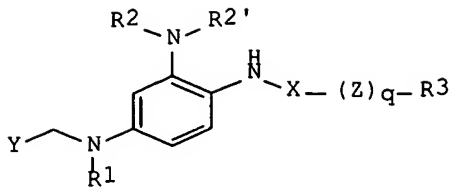
=>

=> d ibib abs hitstr l13 1-2

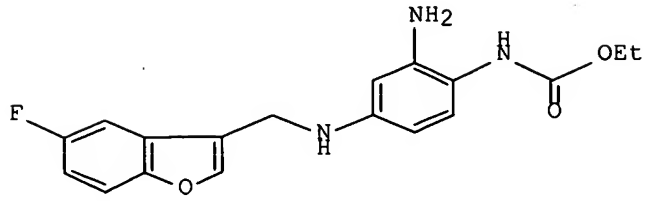
L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:566591 HCAPLUS Full-text
DOCUMENT NUMBER: 141:123466
TITLE: Preparation of 1,2,4-triaminobenzene derivatives useful for treating disorders of the central nervous system
INVENTOR(S): Rottlaender, Mario; Ritzen, Andreas; Bang, Norgaard Morten; Khanzhin, Nikolay; Wenzel, Tornoe Christian
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058739	A1	20040715	WO 2003-DK906	20031218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511502	A1	20040715	CA 2003-2511502	20031218
AU 2003287922	A1	20040722	AU 2003-287922	20031218
EP 1578740	A1	20050928	EP 2003-779762	20031218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017748	A	20051122	BR 2003-17748	20031218
CN 1732162	A	20060208	CN 2003-80107695	20031218
JP 2006515300	T	20060525	JP 2004-562504	20031218
US 2006014822	A1	20060119	US 2005-540075	20050622
NO 2005003612	A	20050923	NO 2005-3612	20050725
PRIORITY APPLN. INFO.:			DK 2002-2012 A	20021227
			US 2002-436697P P	20021227
			WO 2003-DK906 W	20031218

OTHER SOURCE(S): MARPAT 141:123466
GI



I



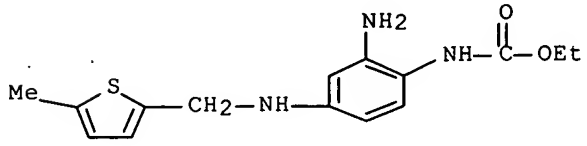
II

AB Title compds. I [R1 = H, alk(en/yn)yl, cycloalk(en)yl, etc.; R2-2' = H, alk(en/yn)yl, aryl, etc.; R3 = H, alk(en/yn)yl, cycloalk(en)yl, aryl, etc.; X = CO, SO2; Z = O, amino; q = 0-1; Y = (benzo)heteroaryl] are prepared For instance, (4-amino-2-nitrophenyl)carbamic acid Et ester is reductively alkylated with 5-Fluorobenzofuran-3-carboxaldehyde (i. o-xylene, Amberlite IRC-84, reflux, 5 h; ii. dioxane/MeOH, NaBH4) and the product reduced (EtOH/HCl, Fe, 60°, 20 min) to give II. I are useful in the treatment of diseases associated with the KCNQ family potassium channels; example compds. have EC50 < 20,000 nM for the KCNQ2 channel.

IT 721943-34-6P, [2-Amino-4-[(5-methylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester dihydrochloride 721943-35-7P, [2-Amino-4-[(3-methylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester dihydrochloride 721943-36-8P, [2-Amino-4-[(thiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester dihydrochloride 721943-37-9P, [2-Amino-4-[(thiophene-3-ylmethyl)amino]phenyl]carbamic acid ethyl ester dihydrochloride 721943-39-1P, [2-Amino-4-[[4-(4-chlorobenzenesulfonyl)-3-methylthiophene-2-ylmethyl]amino]phenyl]carbamic acid ethyl ester 721943-41-5P, [2-Amino-4-[(3-chlorothiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-42-6P, [2-Amino-4-[(4-bromo-3-methoxythiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-46-0P 721943-47-1P 721943-48-2P 721943-49-3P, [2-Amino-4-[(5-fluorothiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-50-6P 721943-51-7P, [2-Amino-4-[(5-bromothiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-52-8P, [2-Amino-4-[(4-bromothiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-53-9P, [2-Amino-4-[(5-ethylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-55-1P, [2-Amino-4-[(5-phenylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-58-4P, N-[2-Amino-4-[(5-chlorothiophene-2-ylmethyl)amino]phenyl]-2-(4-fluorophenyl)acetamide 721943-59-5P, N-[2-Amino-4-[(5-chlorothiophene-2-ylmethyl)amino]phenyl]-3,3-dimethylbutyramide 721943-60-8P, [2-Amino-4-[(5-methylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-61-9P, [2-Amino-4-[(3-methylthiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-62-0P, [2-Amino-4-[(thiophene-2-ylmethyl)amino]phenyl]carbamic acid ethyl ester 721943-63-1P,

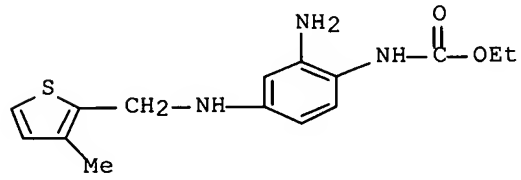
[2-Amino-4-[(thiophene-3-ylmethyl)amino]phenyl]carbamic acid ethyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,4-triaminobenzene derivs. useful for treating disorders of central nervous system)

RN 721943-34-6 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-methyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



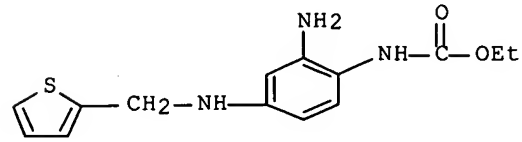
●2 HCl

RN 721943-35-7 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(3-methyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



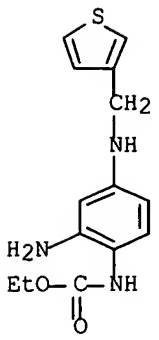
●2 HCl

RN 721943-36-8 HCAPLUS
CN Carbamic acid, [2-amino-4-[(2-thienylmethyl)amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



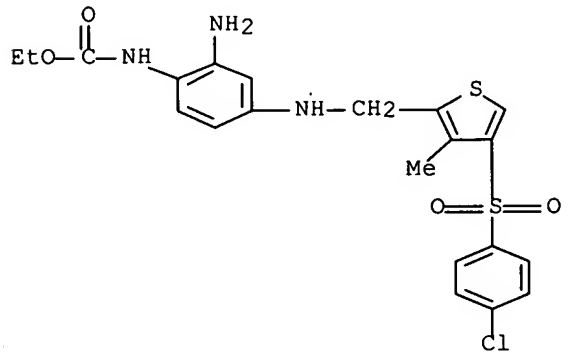
●2 HCl

RN 721943-37-9 HCAPLUS
CN Carbamic acid, [2-amino-4-[(3-thienylmethyl)amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

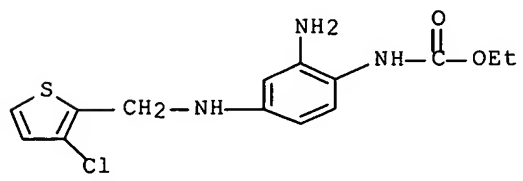


●2 HCl

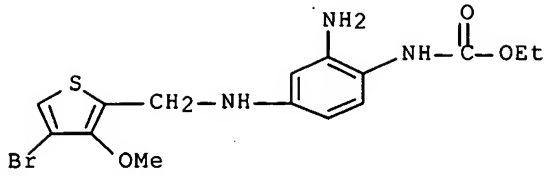
RN 721943-39-1 HCAPLUS
CN Carbamic acid, [2-amino-4-[[[4-[(4-chlorophenyl)sulfonyl]-3-methyl-2-thienyl]methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



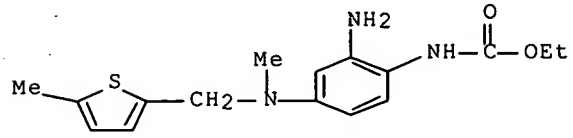
RN 721943-41-5 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(3-chloro-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



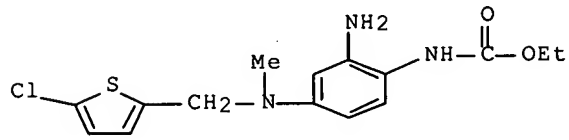
RN 721943-42-6 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(4-bromo-3-methoxy-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



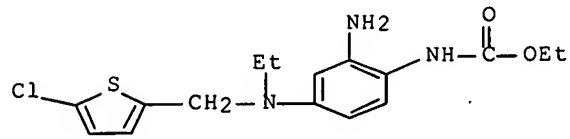
RN 721943-46-0 HCAPLUS
CN Carbamic acid, [2-amino-4-[methyl[(5-methyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



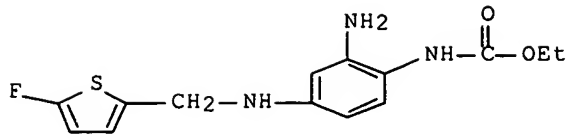
RN 721943-47-1 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-chloro-2-thienyl)methyl]methylamino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



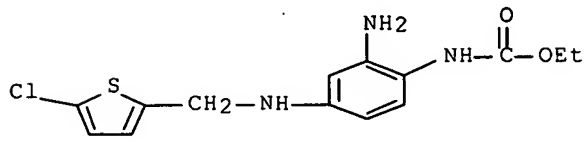
RN 721943-48-2 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-chloro-2-thienyl)methyl]ethylamino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



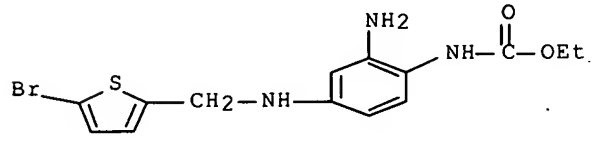
RN 721943-49-3 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-fluoro-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



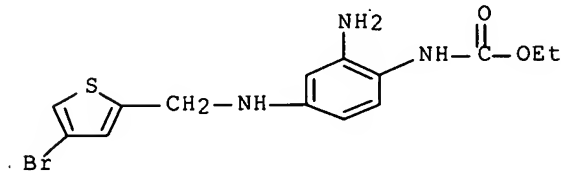
RN 721943-50-6 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-chloro-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



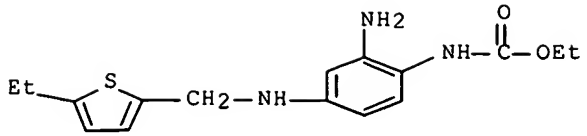
RN 721943-51-7 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-bromo-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



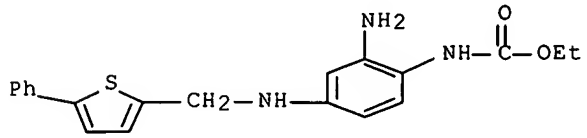
RN 721943-52-8 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(4-bromo-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



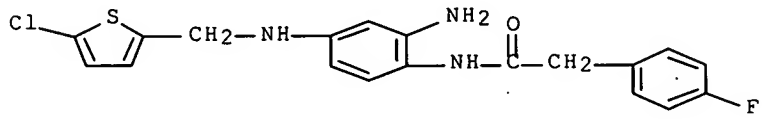
RN 721943-53-9 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-ethyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



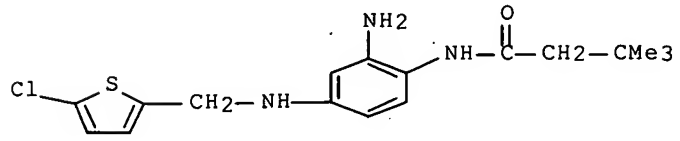
RN 721943-55-1 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-phenyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



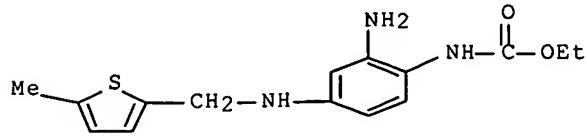
RN 721943-58-4 HCAPLUS
CN Benzeneacetamide, N-[2-amino-4-[[(5-chloro-2-thienyl)methyl]amino]phenyl]-4-fluoro- (9CI) (CA INDEX NAME)



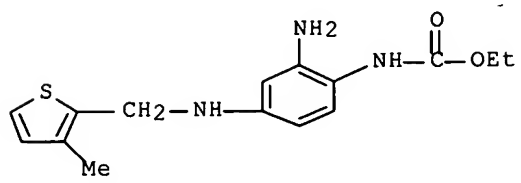
RN 721943-59-5 HCAPLUS
CN Butanamide, N-[2-amino-4-[[(5-chloro-2-thienyl)methyl]amino]phenyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)



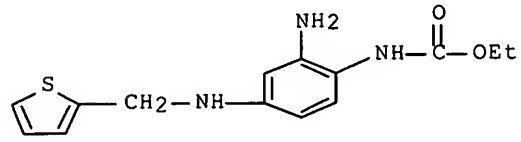
RN 721943-60-8 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(5-methyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



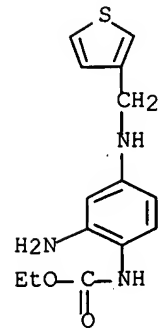
RN 721943-61-9 HCAPLUS
CN Carbamic acid, [2-amino-4-[[(3-methyl-2-thienyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 721943-62-0 HCAPLUS
CN Carbamic acid, [2-amino-4-[(2-thienylmethyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



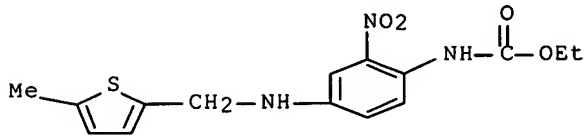
RN 721943-63-1 HCAPLUS
CN Carbamic acid, [2-amino-4-[(3-thienylmethyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



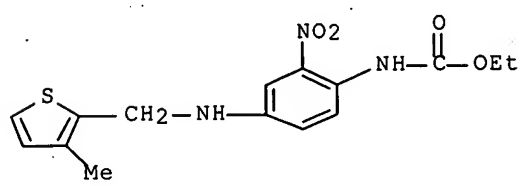
IT 721943-21-1P, [4-[(5-Methylthiophene-2-ylmethyl)amino]-2-nitrophenyl]carbamic acid ethyl ester 721943-22-2P, [4-[(3-Methylthiophene-2-ylmethyl)amino]-2-nitrophenyl]carbamic acid ethyl ester 721943-23-3P, [4-[(Thiophene-2-ylmethyl)amino]-2-nitrophenyl]carbamic acid ethyl ester 721943-24-4P, [4-[(Thiophene-3-ylmethyl)amino]-2-nitrophenyl]carbamic acid ethyl ester 721943-29-9P, N-[4-[(5-Chlorothiophene-2-ylmethyl)amino]-2-nitrophenyl]-2-(4-fluorophenyl)acetamide 721943-31-3P, N-[4-[(5-Chlorothiophene-2-ylmethyl)amino]-2-nitrophenyl]-3,3-dimethylbutyramide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of 1,2,4-triaminobenzene derivs. useful for treating disorders of central nervous system)

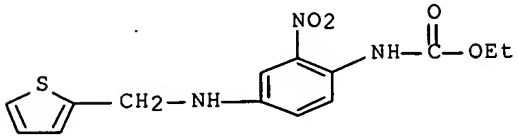
RN 721943-21-1 HCAPLUS
CN Carbamic acid, [4-[[(5-methyl-2-thienyl)methyl]amino]-2-nitrophenyl]-, ethyl ester (9CI) (CA INDEX NAME)



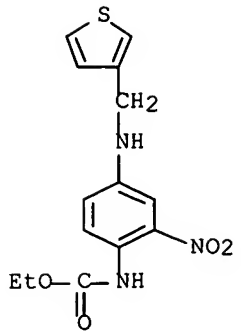
RN 721943-22-2 HCAPLUS
CN Carbamic acid, [4-[[(3-methyl-2-thienyl)methyl]amino]-2-nitrophenyl]-, ethyl ester (9CI) (CA INDEX NAME)



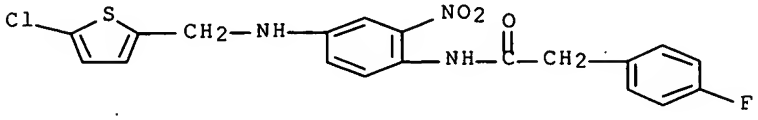
RN 721943-23-3 HCAPLUS
CN Carbamic acid, [2-nitro-4-[(2-thienylmethyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



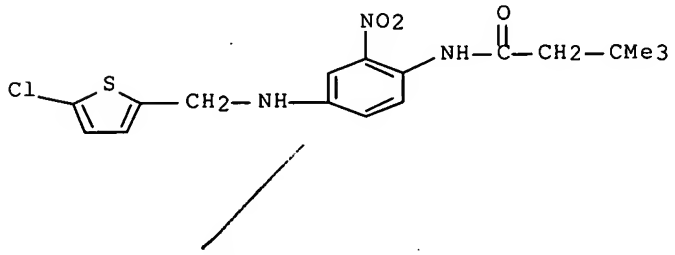
RN 721943-24-4 HCAPLUS
CN Carbamic acid, [2-nitro-4-[(3-thienylmethyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 721943-29-9 HCAPLUS
CN Benzeneacetamide, N-[4-[[(5-chloro-2-thienyl)methyl]amino]-2-nitrophenyl]-4-fluoro- (9CI) (CA INDEX NAME)



RN 721943-31-3 HCAPLUS
CN Butanamide, N-[4-[[(5-chloro-2-thienyl)methyl]amino]-2-nitrophenyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)



L13 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:673452 HCAPLUS Full-text
DOCUMENT NUMBER: 115:273452
TITLE: Aqueous herbicide suspension concentrates for paddy.
INVENTOR(S): Ogawa, Yasuo; Kimura, Fumio; Kimura, Yakira
PATENT ASSIGNEE(S): Ishihara Sangyo Kaisha, Ltd., Japan
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 17 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1050662	A	19910417	CN 1990-107901	19900919
CN 1043502	B	19990602		
JP 03173801	A	19910729	JP 1990-24037	19900202
ES 2032254	A1	19930116	ES 1990-2451	19900925

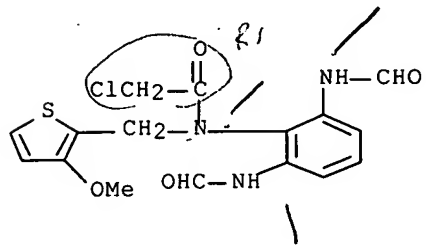
ES 2032254	B1	19940116			
KR 181715	B1	19990401	KR 1990-15338		19900927
PRIORITY APPLN. INFO.:			JP 1989-252853	A	19890928
			JP 1990-24037	A	19900202

AB The title concentrate contains ≥1 herbicide, surfactant, alkane and water. The herbicide is 4-(2,4-dichlorobenzoyl)-1,3-dimethyl-5-benzoylmethoxypyrazole, 4-(2,4-dichlorobenzoyl)-1,3-dimethyl-5-pyrazolyl p-toluenesulfonate, etc. (34 compds. given). The surfactant is nonionic or anionic.

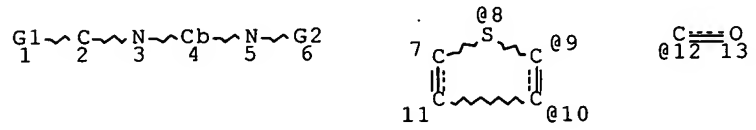
IT 137658-67-4
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(herbicidal composition containing, for paddy)

RN 137658-67-4 HCAPLUS

CN Acetamide, N-[2,6-bis(formylamino)phenyl]-2-chloro-N-[(3-methoxy-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



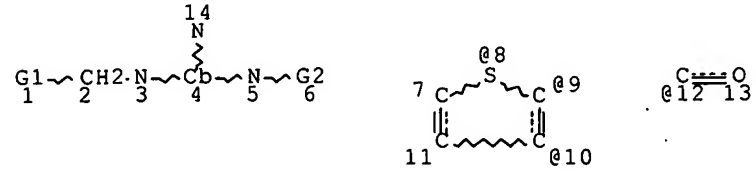
=> => d stat que l20
L1 STR



VAR G1=8/9/10
VAR G2=12/SO2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
L6 2120 SEA FILE=REGISTRY SSS FUL L1
L10 STR



```
VAR G1=8/9/10
VAR G2=12/SO2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  AT   4
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   7
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L12          29 SEA FILE=REGISTRY SUB=L6 SSS FUL L10
L13           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12
L14           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ROTTLANDER MARIO"/AU
L15          23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("RITZEN A"/AU OR "RITZEN
                ANDREAS"/AU)
L16           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NORGAARD M"/AU OR ("NORGAARD
                MORTEN"/AU OR "NORGAARD MORTEN BANG"/AU)
L17           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "KHANZHIN NIKOLAY"/AU
L18          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("TORNOE C"/AU OR "TORNOE C
                W"/AU) OR ("TORNOE CHRISTIAN"/AU OR "TORNOE CHRISTIAN W"/AU)
L19          53 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR L15 OR L16 OR L17 OR
                L18
L20          52 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 NOT L13


=>
=>

=> d ibib abs hitstr l20 1-52

L20  ANSWER 1 OF 52  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:108216  HCAPLUS  Full-text
DOCUMENT NUMBER:         146:219980
TITLE:                   The potential therapeutic use of phosphodiesterase 10
                         inhibitors
AUTHOR(S):               Kehler, Jan; Ritzen, Andreas; Greve, Daniel
                         Rodriguez
CORPORATE SOURCE:        Medicinal Chemistry, Valby, DK-2500, Den.
SOURCE:                  Expert Opinion on Therapeutic Patents (2007), 17(2),
                         147-158
                         CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER:               Informa Healthcare
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
```

AB A review. The discovery of the enzyme phosphodiesterase 10A (PDE10A) was reported simultaneously in 1999 by three independent groups. PDE10A has been shown by localization studies to have the most restricted distribution of all the 11 known PDE families, with the PDE10A mRNA highly expressed only in the brain and testes. In the brain, mRNA and protein are highly enriched in the striatum and, together with increased pharmacol. characterization, this unique distribution of PDE10A in the brain indicates a potential use of PDE10A inhibitors for treating neurol. and psychiatric disorders, in particular, psychotic disorders like schizophrenia. However, PDE10A inhibitors have also been claimed to be useful as treatment for cancer, diabetes and especially obesity. Two years after the reported discovery of PDE10A, Bayer filed the first patent application claiming PDE10A inhibitors, followed shortly

thereafter by Pfizer. Since then, a number of scientific publications and filed patents testify to an increasing pharmaceutical interest in this target. This article highlights and reviews research advances published in the patent literature between the first patent publication in June 2002 and Nov. 2006. The article is supplemented with selected publications from the scientific literature, emphasizing the possible involvement of PDE10A inhibitors in the treatment of schizophrenia and referring to studies aimed at understanding their mechanism and pathophysiol.

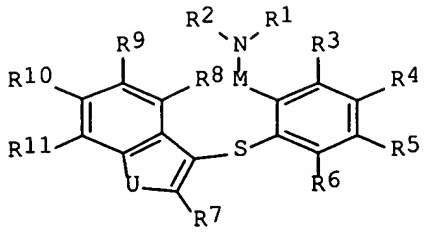
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1339197 HCAPLUS Full-text
DOCUMENT NUMBER: 146:81757
TITLE: Preparation of benzo[b]furan and benzo[b]thiophene derivatives as serotonin, noradrenalin and/or dopamine reuptake inhibitors
INVENTOR(S): Kehler, Jan; Juhl, Karsten; Norgaard, Morten Bang
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 23pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

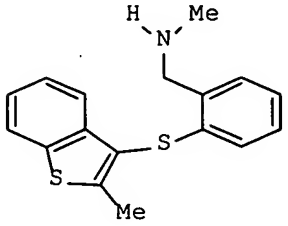
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006287386	A1	20061221	US 2006-452823	20060614
WO 2007023395	A2	20070301	WO 2006-IB3395	20060614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2005-895 A 20050617
OTHER SOURCE(S): MARPAT 146:81757
GI



I



II

AB The present invention relates to the preparation of benzo[b]furan and benzo[b]thiophene derivs. I [U = O or S; R1-2 independently = H, alkenyl, alkynyl, etc.; R3-6 independently = H, halo, CN, etc.; R7 = H, alkenyl, cycloalkenyl, etc.; R8-11 independently = H, CN, haloalkenyl, etc.; M = (X)m(Y)n(Z)o(Q)p; m, n, o and p = 0 or 1; X, Y, Z and Q independently = CH2, CHR12, and CR13R14; R12-14 independently = alkenyl, alkynyl, etc.], and their pharmaceutically acceptable salts, for use as serotonin, noradrenalin and/or dopamine reuptake inhibitors. Thus, e.g., II was prepared by converting intermediate [2-(2-methylbenzo[b]thiophen-3- ylsulfanyl)phenyl]methanol to the mesylate then substitution with Me amine. Methods for bioassays are provided (no data). I is further disclosed for treatment of affective disorders, pain disorders, attention deficit hyperactivity disorder, and stress urinary incontinence.

L20 ANSWER 3 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1339024 HCAPLUS Full-text
DOCUMENT NUMBER: 146:81763
TITLE: Preparation of 2-(1H-indolylsulfanyl)aryl amine derivatives as serotonin, noradrenalin, and/or dopamine reuptake inhibitors
INVENTOR(S): Kehler, Jan; Juhl, Karsten; Norgaard, Morten Bang
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

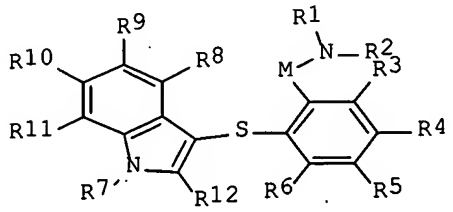
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006134499	A2	20061221	WO 2006-IB2785	20060614

W: AE, AG, AL, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD,

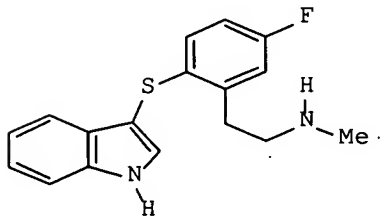
SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

US 2006287382	A1	20061221	US 2006-453022	20060614
PRIORITY APPLN. INFO.:			US 2005-692009P	P 20050617
			DK 2005-894	A 20050617

OTHER SOURCE(S): MARPAT 146:81763
GI



I



II

AB Title compds. I [R1-2 independently = H, alkenyl, alkynyl, etc.; R3-6 and R8-12 independently = H, halo, CN, etc.; R7 = H, alkenyl, cycloalkenyl, etc.; M = (X)m(Y)n(Z)o(Q)p; m-p independently = 0-1 with provision that when m+n+o+p = 1 then none of X, Y, Z and Q = CH2; X, Y, Z and Q = CH2, CHR13 or CR14R15 wherein R13-15 independently = alkenyl, alkynyl, cycloalkenyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as serotonin, noradrenalin, and/or dopamine reuptake inhibitors. Thus, e.g, II was prepared by deprotection of corresponding N-BOC derivative (preparation given). Bioassay methods are described (no data). I is further disclosed for treatment of affective disorders, pain disorders, attention deficit hyperactivity disorder, and stress urinary incontinence.

L20 ANSWER 4 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2006:917475 HCAPLUS Full-text
DOCUMENT NUMBER:	145:315000
TITLE:	Substituted morpholinylpyridine derivatives as potassium channel openers, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S):	Tornoee, Christian Wenzel; Khanzhin, Nikolay ; Rottlaender, Mario; Watson, William Patrick; Greve, Daniel Rodriguez

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 64pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006092143	A1	20060908	WO 2006-DK123	20060302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2005-321 A 20050303
US 2005-658428P P 20050303

OTHER SOURCE(S): MARPAT 145:315000
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to pyridine derivs. of the general formula I, which are openers of the KCNQ family of potassium ion channels. In compds. I, q is 0 or 1; R1 and R2 are independently selected from halo, cyano, C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-6 alkyl, halo-C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; and R3 is selected from C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, C3-8 cycloalkyl, (un)substituted aryl-C1-6 alkyl, (un)substituted aryl-C3-8 cycloalkyl, heteroaryl-C1-6 alkyl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound according to formula I and one or more pharmaceutically acceptable carriers or diluents, as well as to the use of the compns. for the treatment of CNS disorders, such as epilepsy. Heterocyclization of 2-amino-4,6-dimethylpyridine with bis(2-chloroethyl) ether gave morpholinylpyridine II, which underwent nitration, reduction, and acylation with 3-(3-chlorophenyl)propionic acid to give (acylamino)pyridine III. Of the compds. of the invention, many express EC50 values of less than 200 nM in an assay for relative efflux through the KCNQ2 channel (no specific data).
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:402269 HCAPLUS Full-text
DOCUMENT NUMBER: 145:203099
TITLE: Use of postmenopausal hormone replacement therapy and risk of non-Hodgkin's lymphoma: a Danish Population-based Cohort Study
AUTHOR(S): Norgaard, M.; Poulsen, A. H.; Pedersen, L.; Gregersen, H.; Friis, S.; Ewertz, M.; Johnsen, H. E.;

Sorensen, H. T.
CORPORATE SOURCE: Department of Clinical Epidemiology, Aarhus University Hospital, Aalborg, DK-9100, Den.
SOURCE: British Journal of Cancer (2006), 94(9), 1339-1341
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Use of postmenopausal hormone replacement therapy (HRT) has been hypothesised to be associated with a reduced risk of non-Hodgkin's lymphoma (NHL), but the epidemiol. evidence is conflicting. To examine the risk of NHL in HRT users aged 40 and older, we conducted a cohort study in the County of North Jutland, Denmark (population 0.5 million) using data from population-based health registries for the period 1989-2002. We computed age-standardized NHL incidence rates and used Cox regression anal. to compute the relative risk (RR) and corresponding 95% confidence intervals (CI) of NHL among HRT users compared with non-users, adjusting for age and calendar period. The number of prescriptions redeemed (1, 2-4, 5-9, 10-19, or 20 or more prescriptions) was used as a proxy for duration of HRT. We identified 40 NHL cases among HRT users during 179,838 person-years of follow-up and 310 NHL cases among non-users during 1 247,302 person-years of follow-up. The age-standardized incidence rates of NHL were 25.7 per 100,000 among HRT users and 24.2 per 100,000 among non-users, yielding an adjusted RR of 0.99 (95% CI: 0.71-1.39). Our data did not support an association between HRT use and risk of NHL.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:366808 HCAPLUS Full-text
DOCUMENT NUMBER: 145:305508
TITLE: Optimizing Lithium Dosing in Hemodialysis
AUTHOR(S): Bjarnason, N. H.; Munkner, R.; Kampmann, J. P.; Tornoe, C. W.; Ladefoged, S.; Dalhoff, K.
CORPORATE SOURCE: Department of Clinical Pharmacology, Rigshospitalet, Copenhagen, Den.
SOURCE: Therapeutic Drug Monitoring (2006), 28(2), 262-266
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied a 62-yr-old female hemodialysis patient during initiation and maintenance of lithium carbonate therapy. Three different methods were applied to estimate the regimen: a scenario based on volume of distribution (Vd), a scenario based on glomerular filtration rate (GFR), and a scenario in which we developed an algorithm based on a 2-compartment distribution without elimination. The GFR estimate led to plasma concns. 3-4 times lower than those anticipated. In contrast, the ests. based on Vd and the algorithm derived from pharmacokinetic modeling led to comparable loading dose ests. Furthermore, the maintenance dose estimated from the central compartment (V1) led to plasma concns. within the therapeutic range. Thus, a regimen where 12.2 mmol lithium was given after each hemodialysis session resulted in stable between-dialysis plasma lithium concns. in this patient with no residual kidney function. We did not observe adverse effects related to this regimen, which was monitored from 18 days to 8 mo of therapy, and the patient experienced relief from her severe depressive disorder. In conclusion, dialysis patients may be treated with lithium administrated immediately postdialysis. Further observations are necessary to obtain robust long-term safety data and to optimize the monitoring schedule.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:269060 HCAPLUS Full-text
DOCUMENT NUMBER: 144:311786
TITLE: Substituted aniline derivatives as KCNQ subtype potassium ion channel openers, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Tornoee, Christian Wenzel; Rottlaender, Mario; Greve, Daniel Rodriguez; Khanzhin, Nikolay; Ritzen, Andreas; Watson, William Patrick
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006029623	A1	20060323	WO 2005-DK560		20050902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
US 2006155121	A1	20060713	US 2005-312664		20051220
PRIORITY APPLN. INFO.:			DK 2004-1394	A	20040913
			US 2004-609856P	P	20040913
			WO 2005-DK560	A1	20050902

OTHER SOURCE(S): MARPAT 144:311786
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to aniline derivs. of formula I, which are openers of the KCNQ family of potassium ion channels. In compds. I, Z is O or S; q is 0 or 1; R1 and R2 are independently selected from halo, cyano, amino, C1-6 alkyl, C2-6 alkenyl, C3-8 cycloalkyl, C3-8 heterocyclyl, aryl, heteroaryl, etc.; R3 is selected from C1-8 alkyl, C2-8 alkenyl, C3-8 cycloalkyl, aryl-C1-6 alkyl, aryl-C3-8 cycloalkyl, C3-8 heterocyclyl-C1-6 alkyl, heteroaryl-C1-6 alkyl, etc.; and R4 is selected from halo, cyano, C1-6 alkyl, C2-6 alkenyl, C3-8 cycloalkyl, C3-8 heterocyclyl, aryl, heteroaryl, aryl-C1-6 alkyl, (un)substituted amino, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I with one or more pharmaceutically acceptable carriers or diluents, as well as to the use of the compns. for the treatment of a disorder or disease being responsive to an increased ion flow in a potassium channel, such as epilepsy. Amidation of cyclopentaneacetyl chloride with 4-bromo-2,6-dimethylaniline gave acetamide II, which underwent substitution with pyrrole to give acetanilide III. Some

compds. of the invention express EC50 values below 200 nM in an assay for affinity for the KCNQ2 receptor subtype.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1198677 HCAPLUS Full-text
DOCUMENT NUMBER: 143:409564
TITLE: Retrofitted pipe plants
AUTHOR(S): Norgaard, Morten
CORPORATE SOURCE: Germany
SOURCE: Betonwerk + Fertigteil-Technik (2003), 69(10), 58-62
CODEN: BWFTAB; ISSN: 0373-4331
PUBLISHER: BertelsmannSpringer Bauverlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English/German
AB During the past years several new automatic pipe plants have been established or retrofitted in the USA. A large part of the plants have been built up from the ground with the challenges that planning, permission etc. bring. Contrary to these plants other installations have been carried out on the basis of existing buildings with the utmost consideration to partly reduce the extent of the building investments, at the same time making use of earlier investments in production equipment.

L20 ANSWER 9 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1124699 HCAPLUS Full-text
DOCUMENT NUMBER: 143:378927
TITLE: Molecular pharmacology and therapeutic prospects of metabotropic glutamate receptor allosteric modulators
AUTHOR(S): Ritzen, Andreas; Mathiesen, Jesper Mosolff; Thomsen, Christian
CORPORATE SOURCE: Department of Medicinal Chemistry, H. Lundbeck A/S, Research, Valby, Den.
SOURCE: Basic & Clinical Pharmacology & Toxicology (2005), 97(4), 202-213
CODEN: BCPTBO; ISSN: 1742-7835
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The metabotropic glutamate receptors (mGluR) consist of a family of eight G-protein-coupled receptors that differ in their function, distribution and physiol. roles within the central nervous system. In recent years substantial efforts have been made towards developing selective agonists and antagonists which have proven useful for elucidating their potential as novel targets for the treatment of psychiatric and neurol. diseases. In the present review the authors will provide an update of the recent developments of functional allosteric modulators of the mGluR family and explore their therapeutic potential for anxiety/depression, schizophrenia, epilepsy/stroke, pain and Alzheimer's, Parkinson's and Huntington's diseases.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1026943 HCAPLUS Full-text
DOCUMENT NUMBER: 143:306325
TITLE: Substituted morpholine and thiomorpholine derivatives as potassium channel openers, their preparation, pharmaceutical compositions, and use
INVENTOR(S): Wenzel Tornoe, Christian; Rottlaender, Mario;

Khanzhin, Nikolay; Ritzen, Andreas;
Watson, William Patrick
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005087754	A1	20050922	WO 2005-DK159		20050309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2005221762	A1	20050922	AU 2005-221762		20050309
CA 2559397	A1	20050922	CA 2005-2559397		20050309
EP 1727809	A1	20061206	EP 2005-706819		20050309
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
US 2006167248	A1	20060727	US 2005-314802		20051221
PRIORITY APPLN. INFO.:			DK 2004-412	A	20040312
			US 2004-552574P	P	20040312
			WO 2005-DK159	W	20050309

OTHER SOURCE(S): MARPAT 143:306325
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

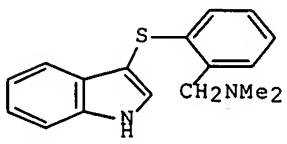
AB The invention relates to morpholine and thiomorpholine derivs. I, which are potassium channel openers. In compds. I, W is O or S; Z is a bond or O; R1 is selected from halo, cyano, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalk(en)yl(oxy), etc.; R2 is selected from halo, cyano, C1-6 alkyl, C3-8 cycloalk(en)yl(oxy), (un)substituted Ph, (un)substituted pyridinyl, etc.; R3 is selected from C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-8 cycloalk(en)yl, aryl-C3-8 cycloalk(en)yl, aryl, etc.; and each of R4, R5, R6, and R7 is independently selected from H and aryl; as the free base or salts thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing one or more of compds. I and one or more pharmaceutically acceptable carriers or diluents, as well as to the use of the compns. for the treatment of a disorder or disease responding to an increased ion flow in a potassium channel. 4-Nitro-2- (trifluoromethyl)aniline underwent ortho-bromination and reduction to give diamine II. II cyclized regioselectively with bis-(2-bromoethyl)ether to give the corresponding morpholine, which was acylated with 4-fluorophenylacetyl chloride resulting in the formation of morpholine derivative III. The compds. of the invention express an EC50 value of less than 20 μM, and in many cases less than 200 nM, in the assay of relative efflux through the KCNQ2 channel.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:588896 HCAPLUS Full-text
DOCUMENT NUMBER: 143:115436
TITLE: 2-(1H-Indolylsulfanyl)benzyl amine derivatives as selective serotonin reuptake inhibitors
INVENTOR(S): Kehler, Jan; Juhl, Karsten; Sejberg, Jimmy; Norgaard, Morten Bang
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005061455	A1	20050707	WO 2004-DK894		20041221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004303461	A1	20050707	AU 2004-303461		20041221
CA 2551168	A1	20050707	CA 2004-2551168		20041221
EP 1701940	A1	20060920	EP 2004-803045		20041221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
CN 1898204	A	20070117	CN 2004-80038470		20041221
US 2006160880	A1	20060720	US 2005-314702		20051221
PRIORITY APPLN. INFO.:			DK 2003-1923	A	20031223
			US 2003-532593P	P	20031223
			WO 2004-DK894	W	20041221

OTHER SOURCE(S): MARPAT 143:115436
GI



I

AB The present invention relates to the title compds. and their use as serotonin reuptake inhibitors and preferably also norepinephrine reuptake inhibitors in the treatment of depression, anxiety, affective disorders, pain disorders, attention deficit hyperactivity disorder (ADHD) and stress urinary

incontinence. 2-(1H-indol-3-ylsulfanyl)-N,N-dimethylbenzamide was reduced with borane in THF to give I. Biol. testing data include measurements of [3H]-5-HT uptake and [3H]noradrenaline uptake into rat cortical synaptosomes.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:254835 HCAPLUS Full-text
DOCUMENT NUMBER: 143:400
TITLE: Metronidazole and risk of acute pancreatitis: a population-based case-control study
AUTHOR(S): Norgaard, M.; Ratanajamit, C.; Jacobsen, J.; Skriver, M. V.; Pedersen, L.; Sorensen, H. T.
CORPORATE SOURCE: Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus C, Den.
SOURCE: Alimentary Pharmacology and Therapeutics (2005), 21(4), 415-420
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Use of metronidazole has been suggested to be associated with an increased risk of acute pancreatitis in case reports. To examine this issue within a proper epidemiol. design. We identified 3083 incident cases of acute pancreatitis from Hospital Discharge Registries in three Danish counties and 30 830 matched population controls. From prescription databases, we extracted information on use of metronidazole with or without concomitant use of proton-pump inhibitors and/or amoxicillin, macrolides or tetracycline. Adjusted odds ratios for acute pancreatitis in study subjects who redeemed a prescription for metronidazole within 30, 31-180, or 181-365 days before hospitalization or index date among controls were 3.0 [95% confidence interval (CI): 1.4-6.6], 1.8 (95% CI: 1.2-2.9) and 1.1 (95% CI: 0.6-1.8), resp. Among subjects with a concomitant prescription for proton-pump inhibitors and/or amoxicillin, macrolides or tetracycline within 30, 31-180, or 181-365 days before hospitalization, or index date among controls, adjusted odds ratios were 8.3 (95% CI: 2.6-26.4), 2.7 (95% CI: 1.4-5.5), and 1.7 (95% CI: 0.6-4.8), resp. Metronidazole may increase the risk of acute pancreatitis. However, the risk seems mainly to increase when metronidazole is used in combination with other drugs used for Helicobacter pylori eradication.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

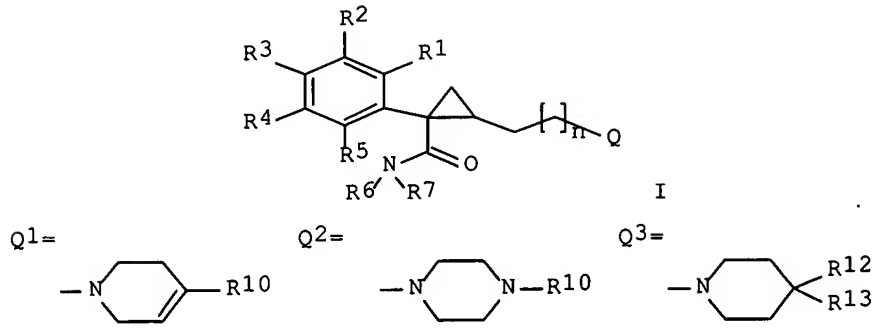
L20 ANSWER 13 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:158639 HCAPLUS Full-text
DOCUMENT NUMBER: 142:261403
TITLE: Preparation of 1-phenylcyclopropane-1-carboxamide derivatives as tachykinin NK3 receptor antagonists
INVENTOR(S): Kehler, Jan; Hansen, Tore; Poulsen, Anders; Bjornholm, Berith; Ruhland, Thomas; Norgaard, Morten Bang ; Nielsen, Soren Moller
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005016884	A1	20050224	WO 2004-DK538		20040813
WO 2005016884	A9	20060316			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004265020	A1	20050224	AU 2004-265020		20040813
CA 2535646	A1	20050224	CA 2004-2535646		20040813
EP 1656349	A1	20060517	EP 2004-739035		20040813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004013584	A	20061017	BR 2004-13584		20040813
CN 1867549	A	20061122	CN 2004-80029691		20040813
JP 2007502253	T	20070208	JP 2006-522897		20040813
NO 2006001137	A	20060309	NO 2006-1137		20060309
US 2006281746	A1	20061214	US 2006-568483		20060814
PRIORITY APPLN. INFO.:			DK 2003-1175	A	20030815
			US 2003-501535P	P	20030908
			WO 2004-DK538	W	20040813

OTHER SOURCE(S): MARPAT 142:261403

GI



AB The present invention relates to cyclopropyl derivs. of formula (I) or salts thereof such as pharmaceutically acceptable salts [wherein R1-R5 = independently H, halogen, cyano, nitro, C1-6 alk(en/yn)yl, C3-8 cycloalk(en)yl, C3-8 cycloalk(en)yl-C1-6-alk(en/yn)yl, amino, C1-6 alk(en/yn)ylamino, di[C1-6-alk(en/yn)yl]amino, C1-6 alk(en/yn)ylcarbonyl, aminocarbonyl, C1-6-alk(en/yn)ylaminocarbonyl, di[C1-6 alk(en)yl]aminocarbonyl, hydroxy, C1-6 alk(en/yn)yloxy, C1-6-alk(en/yn)ylthio, halo-C1-6 alk(en/yn)yl, halo-C1-6 alk(en/yn)ylsulfonyl, halo-C1-6 alk(en/yn)ylsulfanyl, and C1-6 alk(en/yn)ylsulfonyl; R6 = H, halo-C1-6 alk(en/yn)yl, C1-6 alk(en/yn)yl, C3-8 cycloalk(en)yl, C3-8 cycloalk(en)yl-C1-6 alk(en/yn)yl; R7 = aryl, heteroaryl, aryl-CR8R9- (wherein R8, R9 = H, C1-6 alk(en/yn)yl, C3-8 cycloalk(en)yl, C3-8 cycloalk(en)yl-C1-6 alk(en/yn)yl); n =

0-2; Q = Q1, Q2, Q3, etc.; R10, R12 = aryl; R11 = aryl, benzyl, halo-C1-6 alk(en/yn)ylsulfonyl, C1-6 alk(en/yn)ylsulfonyl, arylsulfonyl, arylacyl, C1-6-alk(en/yn)ylcarbonyl, aminocarbonyl, etc.; R13 = H, HO, cyano, or NH2, etc.]. These compds. are NK3 receptor antagonists and may therefore be useful for treatment of diseases where the NK3 receptor is implicated, including psychotic disorders, schizophrenia, depression, anxiety, Parkinson's disease, pain, convulsions, cough, asthma, airway hyperresponsiveness, microvascular hypersensitivity, bronchoconstriction, gut inflammation, inflammatory bowel disease, hypertension, imbalances in water and electrolyte homeostasis, ischemia, edema, plasma extravasation, and obesity. For example, (1S,2R)-2-(4-acetylamino-4-phenylpiperidin-1- ylmethyl)-1-(3,4-dichlorophenyl)cyclopropanecarboxylic acid N-benzyl-N-methylamide had an apparent NK3 affinity (Ki) of less than 50 nM in using a membrane prepared from baby hamster cells stably expressing the human NK3 receptor.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:965219 HCAPLUS Full-text

DOCUMENT NUMBER: 141:395417

TITLE: Preparation of substituted indoline and indole derivatives as openers of the KCNQ family potassium channels

INVENTOR(S): Khanzhin, Nikolay; Rottlaender, Mario; Watson, William Patrick

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.

SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096767	A1	20041111	WO 2004-DK283	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004233941	A1	20041111	AU 2004-233941	20040423
CA 2523102	A1	20041111	CA 2004-2523102	20040423
EP 1631546	A1	20060308	EP 2004-729044	20040423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009317	A	20060425	BR 2004-9317	20040423
CN 1777582	A	20060524	CN 2004-80011019	20040423
JP 2006524641	T	20061102	JP 2006-504366	20040423
NO 2005005562	A	20051124	NO 2005-5562	20051124
US 2006264496	A1	20061123	US 2006-551738	20060207
PRIORITY APPLN. INFO.:			DK 2003-631	A 20030425
			US 2003-465387P	P 20030425
			WO 2004-DK283	W 20040423

PATENT ASSIGNEE(S): Pedershaab Concrete Technologies A/s, Den.
SOURCE: PCT Int. Appl.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062867	A1	20040729	WO 2004-DK2	20040107
WO 2004062867	B1	20040910		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
DK 2003000013	A	20040711	DK 2003-13	20030110
DK 175871	B1	20050502		
EP 1590142	A1	20051102	EP 2004-700440	20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006033227	A1	20060216	US 2005-540235	20050621

PRIORITY APPLN. INFO.: DK 2003-13 A 20030110
WO 2004-DK2 W 20040107

AB A method and an apparatus for the manufacture of concrete pipes (2) comprising an outer layer, said outer layer forming the pipe (2) itself, as well as an inner layer of greater d. in surface structure, said inner layer being applied by an applicator in a mold (1) comprising both outer (3) and inner (4) mold parts, said applicator being formed by an inner mold part or core (4) or by an applicator unit in immediate connection with the core (4), said applicator applying the inner layer during simultaneous or during immediately following vibration, said inner layer being applied during movement of the inner mold part or core (4) in its longitudinal direction, in which core one or more supply openings (14) are provided along the circumference of the core (4) at the upper end of the core (4) for the supply of a further material.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:468595 HCAPLUS Full-text
DOCUMENT NUMBER: 142:156289
TITLE: Pyrazines on solid support from peptides by periodinane oxidation of threonine side-chains. A quantitative chemical transformation (QCT) for combinatorial chemistry
AUTHOR(S): Christensen, Caspar; Tornoe, Christian W.; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: QSAR & Combinatorial Science (2004), 23(2-3), 109-116
CODEN: QCSSAU; ISSN: 1611-020X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:156289
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The β-hydroxymethylene in threonine residues adjacent to an N-terminal amino acid were subjected to oxidation effected by Dess-Martin periodinane on solid support. Fmoc-cleavage at the N-terminal amino acid afforded 3,6-dihydro-1H-pyrazin-2-one, which oxidized spontaneously to the 1H-pyrazin-2-ones I (R is an amino acid side chain). A variety of naturally occurring and synthetic α-amino acids gave rise to a diverse subset of functionalized 1H-pyrazin-2-ones. An amino functionality in the side-chain of the N-terminal amino acid residue allowed elongation by conventional solid phase peptide chemical, yielding II (n = 1 or 4). Furthermore, elongation of the side-chain with Thr and a second amino acid followed by oxidation afforded bis-1H-pyrazin-2-one III in high yield.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 18 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267885 HCAPLUS Full-text
DOCUMENT NUMBER: 141:401
TITLE: Combinatorial Library of Peptidotriazoles: Identification of [1,2,3]-Triazole Inhibitors against a Recombinant Leishmania mexicana Cysteine Protease
AUTHOR(S): Tornoe, Christian W.; Sanderson, Sanya J.; Mottram, Jeremy C.; Coombs, Graham H.; Meldal, Morten
CORPORATE SOURCE: Center for Solid-Phase Organic Combinatorial Chemistry, Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Journal of Combinatorial Chemistry (2004), 6(3), 312-324
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:401

AB A library consisting of about half of 800 000 possible peptidotriazoles on 450 000 beads was prepared by solid-phase peptide synthesis combined with a regiospecific copper(I)-catalyzed 1,3-dipolar cycloaddn. between a resin-bound alkyne and a protected amino azide. The central [1,2,3]-triazole was flanked on each side by two randomized amino acids introduced in a combinatorial approach. Importantly, the formation of the triazole could be performed quant. in a randomized fashion. The library was screened on solid phase for inhibitory effect against a recombinant cysteine protease, Leishmania mexicana CPB2.8ΔCTE and sorted by a high-throughput instrument, COPAS beadsorter (up to 200 000 beads/h). Forty-eight hits were analyzed by MALDI-TOF MS providing structural information about the protease specificity, and 23 peptidotriazoles were resynthesized and evaluated in solution, with the best inhibitor displaying a Ki value of 76 nM. A one-pot procedure was used to convert Fmoc-amino azides into their corresponding Boc derivs. The crucial influence of weak interactions with a spacer used for detection by MALDI-TOF MS on screening results was observed

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 19 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:173709 HCAPLUS Full-text
DOCUMENT NUMBER: 141:116419
TITLE: Interaction of Epothilone Analogs with the Paclitaxel Binding Site Relationship between Binding Affinity, Microtubule Stabilization, and Cytotoxicity

AUTHOR(S): Buey, Ruben M.; Diaz, J. Fernando; Andreu, Jose M.; O'Brate, Aurora; Giannakakou, Paraskevi; Nicolaou, K. C.; Sasmal, Pradip K.; Ritzen, Andreas; Namoto, Kenji

CORPORATE SOURCE: Consejo Superior de Investigaciones Cientificas, Centro de Investigaciones Biologicas, Madrid, 28040, Spain

SOURCE: Chemistry & Biology (2004), 11(2), 225-236
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interactions of epothilone analogs with the paclitaxel binding site of microtubules were studied. The influence of chemical modifications in the C15 side chain and in C12 on binding affinity and microtubule elongation was characterized. Modifications favorable for binding affinity are (1) a thiomethyl group at C21 of the thiazole side chain, (2) a Me group at C12 in S configuration, (3) a pyridine side chain with C15 in S configuration, and (4) a cyclopropyl moiety between C12 and C13. The same modification in different ligands has similar effect on affinity, allowing good structure-affinity characterization. The correlation between binding, microtubule stabilization, and cytotoxicity of the compds. has been determined, showing differential effects of the modifications. The binding consts. correlate well with IC50 values, demonstrating that affinity measurements are a useful tool for drug design.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 20 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:162465 HCAPLUS Full-text

DOCUMENT NUMBER: 140:199143

TITLE: Preparation of cyclopropyl and cyclobutyl epothilone analogs as antitumor agents and potent tubulin polymerization promoters

INVENTOR(S): Nicoloou, Kyriacos C.; Namoto, Kenji; Ritzen, Andreas; Shoji, Mitsuru; Ulven, Trond; Altmann, Karl-Heinz

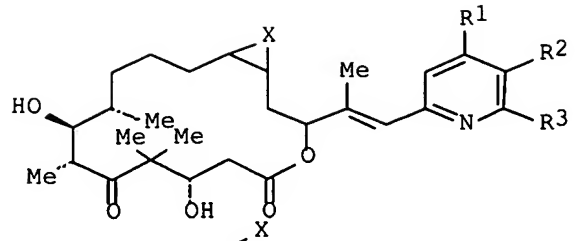
PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: U.S. Pat. Appl. Publ., 35 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

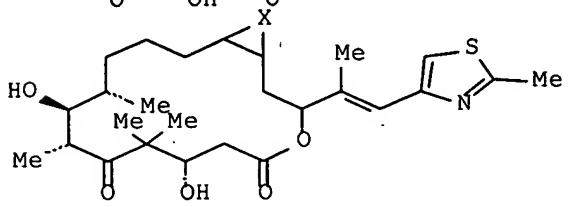
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004039026	A1	20040226	US 2002-227073	20020823
PRIORITY APPLN. INFO.:			US 2002-227073	20020823

OTHER SOURCE(S): MARPAT 140:199143

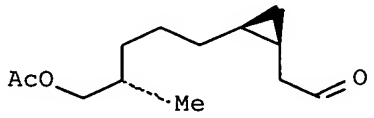
GI



I



II



III

AB Cis- and trans-12, 13-cyclopropyl and 12,13-cyclobutyl epothilones I (X = CH2, CH2CH2; R1 = fused ring structure with R2, C1-C6 alkane; R2 = fused ring structure with R1 or R3, C1-C6 alkane) or II (X = CH2, CH2CH2) were prepared as potent tubulin polymerization promoters and cytotoxic agents for use as anticancer agents. Thus, III was subjected to Nozaki-Hiyama-Kishi coupling, an aldol reaction and Yamaguchi lactonization followed by deprotection to yield II (X = CH2) with an IC50 of 1.60 nM against 1A9 human ovarian carcinoma cells. As well, 83% of tubulin polymerized after incubation with 3 μM of II (X = CH2).

L20 ANSWER 21 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:143161 HCAPLUS Full-text
DOCUMENT NUMBER: 140:181252
TITLE: Preparation and formulation of epothilone B derivatives as antitumor agents
INVENTOR(S): Namoto, Kenji; Nicolaou, Kyriacos Costa; Ritzen, Andreas
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh; The Scripps Research Institute
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014919	A1	20040219	WO 2003-EP8554	20030801

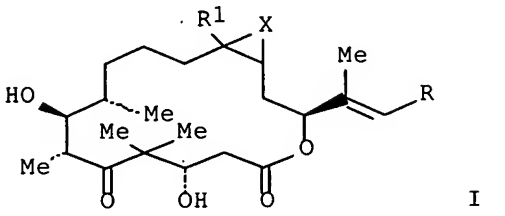
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,

SI, SK, TR

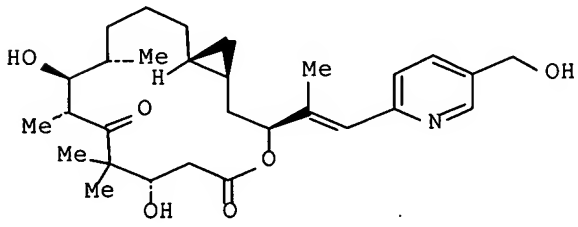
CA 2494259	A1	20040219	CA 2003-2494259		20030801
AU 2003266961	A1	20040225	AU 2003-266961		20030801
EP 1546152	A1	20050629	EP 2003-747872		20030801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013198	A	20050712	BR 2003-13198		20030801
CN 1675220	A	20050928	CN 2003-818644		20030801
JP 2006503814	T	20060202	JP 2004-526852		20030801
US 2004072870	A1	20040415	US 2003-634537		20030804
US 7169930	B2	20070130			
US 2006293527	A1	20061228	US 2006-511610		20060828
PRIORITY APPLN. INFO.:			US 2002-400535P	P	20020802
			US 2003-480933P	P	20030624
			WO 2003-EP8554	W	20030801
			US 2003-634537	A1	20030804

OTHER SOURCE(S): MARPAT 140:181252

GI



I



II

AB Epothilone B derivs. of formula I [R = (substituted) heterocyclyl; R1 = H, Me; X = O, CH2] are prepared for the treatment of proliferative diseases, such as a tumor. Pharmaceutical compns. containing I are described. Thus, II was prepared, and had IC50 of 0.7 against 1A9 human ovarian carcinoma cells.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 22 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:782650 HCAPLUS Full-text

DOCUMENT NUMBER: 140:5178

TITLE: Total synthesis of 1-O-methyllateriflorone

AUTHOR(S): Nicolaou, K. C.; Sasmal, Pradip K.; Xu, Hao; Namoto, Kenji; Ritzen, Andreas

CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Angewandte Chemie, International Edition (2003), 42(35), 4225-4229
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:5178
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The authors report the total synthesis of 1-O-methyllateriflorone using prenylated 2,2'-dimethylbenzopyran fragment I and cage ring system II as starting materials. After preparation of II from benzenoid III, II was then reacted with 4-MeC6H4SO3H, Dess-Martin periodinane, NaClO2, and I/4-DMAP to give a compound which was converted to quinone IV. Exposure of IV to pyridinium p-toluenesulfonate in refluxing benzene gave the title compound in 83% yield.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

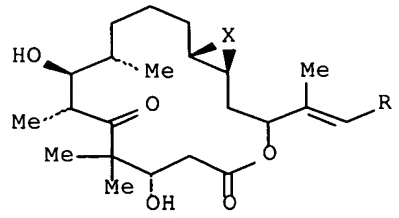
L20 ANSWER 23 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:509497 HCAPLUS Full-text
DOCUMENT NUMBER: 140:164542
TITLE: EXPO3000 - a new expandable polymer for organic synthesis and enzymatic assays
AUTHOR(S): Tornoe, Christian W.; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 281-282. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. EXPO3000 is a copolymer of PEG3000 bis(3-methyloxetan-3-ylmethyl ether) with tetrakis[4-(3-methyloxetan-3- ylmethyl)phenyl]silane which has low swelling in solvents ranging from polar to nonpolar and could be expanded by cleaving a crosslinking unit within the resin. It is well suited to organic synthesis before swelling, whereas the high swelling after expansion makes it suitable for on-bead enzymic assays.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:173421 HCAPLUS Full-text
DOCUMENT NUMBER: 138:221391
TITLE: Synthesis of cyclopropyl and cyclobutyl epothilone analogs and their antitumor and tubulin polymerization inhibitory activities
INVENTOR(S): Nicolaou, Kyriacos Costa; Namoto, Kenji; Ritzen, Andreas; Ulven, Trond; Shoji, Mutsuru; Altmann, Karl-heinz
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.; The Scripps Research Institute; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018002	A2	20030306	WO 2002-EP9407	20020822
WO 2003018002	A3	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
CA 2456280	A1	20030306	CA 2002-2456280	20020822
EP 1420780	A2	20040526	EP 2002-767418	20020822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012107	A	20040824	BR 2002-12107	20020822
CN 1545411	A	20041110	CN 2002-816441	20020822
JP 2005501107	T	20050113	JP 2003-522522	20020822
PRIORITY APPLN. INFO.:			US 2001-314698P P	20010823
			WO 2002-EP9407 W	20020822

OTHER SOURCE(S): MARPAT 138:221391
GI



I

AB The authors synthesized cis- and trans-12,13-cyclopropyl and 12,13-cyclobutyl epothilone analogs, e.g. I [R = 2-methyl-4-thiazolyl, 5-methyl-2-pyridyl, X = (CH2)n, n = 1,2], using aldol, Nozaki-Hiyama-Kishi coupling, and Yamaguchi macrolactonization reactions. Thus, the Nozaki-Hiyama-Kishi coupling reaction was used to attach the thiazolylpropenyl segment. These derivs. were tested for cytotoxicity against human ovarian carcinoma cell lines as well as human epidermoid cancer cell lines and β-tubulin mutant cell lines. The activity promoting tubulin polymerization was also examined Trans-I (R = 5-methyl-2-pyridyl, X = CH2) showed outstanding activity against all the cell lines, with IC50 = 0.6 nM in the human ovarian carcinoma cell line. Some of the compds. display a similar cytotoxicity profile against the β-tubulin mutants compared to epothilone A.

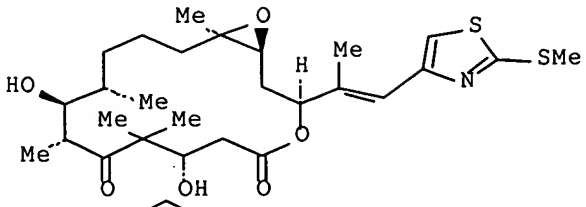
L20 ANSWER 25 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:692341 HCAPLUS Full-text
DOCUMENT NUMBER: 138:385696
TITLE: Peptidotriazoles: copper(I)-catalyzed 1,3-dipolar cycloadditions on solid-phase

AUTHOR(S): Tornoe, Christian W.; Meldal, Morten
CORPORATE SOURCE: Center for Solid Phase Organic Combinatorial Chemistry, Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 263-264. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Peptidotriazoles were prepared via Cu(I)-catalyzed 1,3-dipolar cycloaddn. reactions of HC.tplbond.CCO-FGFG-resin with azides.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

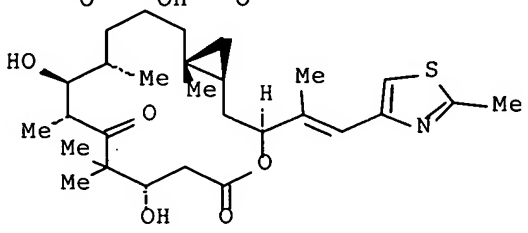
L20 ANSWER 26 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:640963 HCAPLUS Full-text
DOCUMENT NUMBER: 137:353702
TITLE: EXPO3000-a new expandable polymer for synthesis and enzymatic assays
AUTHOR(S): Tornoe, Christian W.; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Center for Solid Phase Organic Combinatorial Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Tetrahedron Letters (2002), 43(36), 6409-6411
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new polymer for synthesis and enzymic assays is presented which combines moderate loading with the biocompatibility of poly(ethylene glycol)-based resins. The polymer was prepared by copolymn. of oxetane terminated polyethylene glycol and a silane having 4 benzyl oxetane groups. The polymer displays low swelling in all solvents until selective cleavage of a silyl based crosslinker expands the polar resin to render it penetratable for enzymes (an example with a 27 kDa protease is given). An efficient alkylation procedure for derivatization of long PEG-chains is also presented.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 27 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:585469 HCAPLUS Full-text
DOCUMENT NUMBER: 137:310727
TITLE: Chemical synthesis and biological evaluation of novel epothilone B and trans-12,13-cyclopropyl epothilone B analogues
AUTHOR(S): Nicolaou, K. C.; Ritzen, Andreas; Namoto, Kenji; Buey, Ruben M.; Diaz, J. Fernando; Andreu, Jose M.; Wartmann, Markus; Altmann, Karl-Heinz; O'Brate, Aurora; Giannakakou, Paraskevi
CORPORATE SOURCE: Department of Chemistry and Skaggs Institute for Chemical Biology, Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Tetrahedron (2002), 58(32), 6413-6432
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:310727
GI



I



II

AB In addition to the total synthesis of the thiomethyl thiazole side chain analog of epothilone B I, a series of related trans-12,13-cyclopropyl epothilone B analogs, e.g. II, was accomplished. While the synthesis of the epothilone B analog I proceeded through a Stille coupling of a vinyl iodide substrate containing the epothilone macrocycle with the appropriate side chain stannane, that of the cyclopropyl analogs involved a convergent strategy in which a Nozaki-Hiyama-Kishi coupling was used as a means of introducing the side chains prior to Yamaguchi macrolactonization and final elaboration to the target mols. The synthesized analogs were subjected to biol. evaluation involving in vitro tubulin polymerization, affinity for the microtubule Taxol binding site and cell cytotoxicity assays. The results identified the methylthio thiazole side chain as a potency enhancing moiety for the epothilones and shed further light on the structure-activity relationships within this important class of chemotherapeutic agents.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 28 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:418516 HCAPLUS Full-text
DOCUMENT NUMBER: 137:139391
TITLE: Biotechnology and combinatorial chemistry
AUTHOR(S): Tornoe, Christian W.; Christensen, Caspar; Meldal, Morten
CORPORATE SOURCE: SPOCC, Carlsberg Laboratorium, Den.
SOURCE: Dansk Kemi (2002), 83(5, Suppl.), 24-26
CODEN: DAKEAT; ISSN: 0011-6335
PUBLISHER: TechMedia
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Danish
AB A review.

L20 ANSWER 29 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:243712 HCAPLUS Full-text
DOCUMENT NUMBER: 137:6388
TITLE: Peptidotriazoles on Solid Phase: [1,2,3]-Triazoles by

Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of Terminal Alkynes to Azides

AUTHOR(S): Tornoe, Christian W.; Christensen, Caspar; Meldal, Morten

CORPORATE SOURCE: Center for Solid Phase Organic Combinatorial Chemistry Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.

SOURCE: Journal of Organic Chemistry (2002), 67(9), 3057-3064
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:6388

AB The cycloaddn. of azides to alkynes is one of the most important synthetic routes to 1H-[1,2,3]-triazoles. This work reports a novel regiospecific copper(I)-catalyzed 1,3-dipolar cycloaddn. of terminal alkynes to azides on solid-phase. Primary, secondary, and tertiary alkyl azides, aryl azides, and an azido sugar were used successfully in the copper(I)-catalyzed cycloaddn. producing diversely 1,4-substituted [1,2,3]-triazoles in peptide backbones or side chains. The reaction conditions were fully compatible with solid-phase peptide synthesis on polar supports. The copper(I) catalysis is mild and efficient (>95% conversion and purity in most cases) and furthermore, the x-ray structure of 2-azido-2-methylpropanoic acid has been solved, to yield structural information on the 1,3-dipoles entering the reaction. Novel Fmoc-protected amino azides were prepared from Fmoc-amino alcs. by Mitsunobu reaction.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 30 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:627684 HCAPLUS Full-text

DOCUMENT NUMBER: 135:344304

TITLE: Chemical synthesis and biological evaluation of cis- and trans-12,13-cyclopropyl and 12,13-cyclobutyl epothilones and related pyridine side chain analogues

AUTHOR(S): Nicolaou, K. C.; Namoto, Kenji; Ritzen, Andreas; Ulven, Trond; Shoji, Mitsuru; Li, Jim; D'Amico, Gina; Liotta, Dennis; French, Christopher T.; Wartmann, Markus; Altmann, Karl-Heinz; Giannakakou, Paraskevi

CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Journal of the American Chemical Society (2001), 123(38), 9313-9323
CODEN: JACSAT; ISSN: 0002-7863

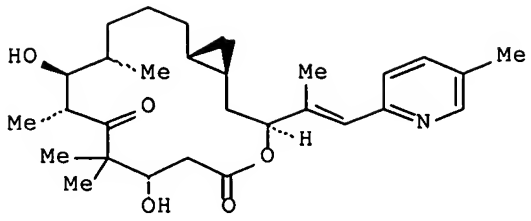
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:344304

GI



I

AB The design, chemical synthesis, and biol. evaluation of a series of cyclopropyl and cyclobutyl epothilone analogs are described. The synthetic strategies toward these epothilones involved a Nozaki-Hiyama-Kishi coupling to form the C15-C16 carbon-carbon bond, an aldol reaction to construct the C6-C7 carbon-carbon bond, and a Yamaguchi macrolactonization to complete the required skeletal framework. Biol. studies with the synthesized compds. led to the identification of 6 epothilone analogs as potent tubulin polymerization promoters and cytotoxic agents with (12R,13S,15S)-cyclopropyl 5-methylpyridine epothilone A (I) as the most powerful compound whose potencies (e.g. IC50 = 0.6 nM against the 1A9 ovarian carcinoma cell line) approach those of epothilone B. These investigations led to a number of important structure-activity relationships, including the conclusion that neither the epoxide nor the stereochem. at C12 are essential, while the stereochem. at both C13 and C15 are crucial for biol. activity. These studies also confirmed the importance of both the cyclopropyl and 5-methylpyridine moieties in conferring potent and potentially clin. useful biol. properties to the epothilone scaffold.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:603086 HCAPLUS Full-text

DOCUMENT NUMBER: 136:47797

TITLE: Recent developments in the chemistry, biology and medicine of the epothilones

AUTHOR(S): Nicolaou, K. C.; Ritzen, Andreas; Namoto, Kenji

CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Chemical Communications (Cambridge, United Kingdom) (2001), (17), 1523-1535
CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal; General Review

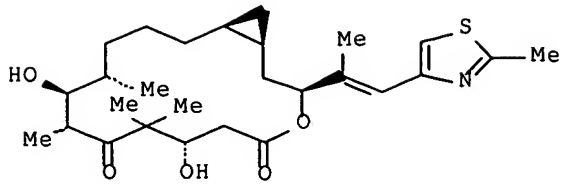
LANGUAGE: English

AB A review. The epothilones have occupied center stage on the scenes of total synthesis, chemical biol. and medicine for the last five years, no doubt because of their intriguing mode of action and unusually high potency against tumor cells, including multidrug-resistant cell lines. This article reviews the most recent advances within this exciting field. Thus, an overview of recent synthetic endeavors culminating in a new generation of total syntheses and analogs, some with higher potencies than the naturally occurring substances, will be given, and the chemical biol., in particular the current understanding of structure-activity relationships of the epothilones, will also be discussed in light of the latest biol. results. In addition, the recently elucidated biosynthetic machinery of the natural epothilone-producing

myxobacterium Sorangium cellulosum, as it is now understood, will be described. Finally, some preclin. and clin. studies will be summarized.
REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 32 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:537234 HCAPLUS Full-text
DOCUMENT NUMBER: 135:318689
TITLE: Synthesis and conformational studies of a 1,1'-ferrocenophane lactam mimetic of substance P
AUTHOR(S): Maricic, Suzana; Ritzen, Andreas; Berg, Ulf; Frejd, Torbjoern
CORPORATE SOURCE: Department of Chemistry, Organic Chemistry 1, Centre for Chemistry and Chemical Engineering, Lund University, Lund, SE-22100, Swed.
SOURCE: Tetrahedron (2001), 57(30), 6523-6529
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:318689
AB The synthesis of a bis-phenylalanine mimetic (I) and its incorporation into Substance P (SP), giving a conformationally constrained organometallic SP analog (II), is described. The lactam I was synthesized in five steps, via a Horner-Wadsworth-Emmons olefination reaction, enantioselective hydrogenation with [Rh(I)(COD)((S,S)Et-DuPHOS)]+OTf- and intramol. cyclization with PyAOP as a coupling reagent. Comparative CD studies of II with native SP indicated that the flexibility around the amide bond of Phe(7)-Phe(8) sequence is crucial for the C-terminal (from residue Gln(4)) to adopt an α-helical conformation in the micellar environment created by SDS or in methanol.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 33 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:52914 HCAPLUS Full-text
DOCUMENT NUMBER: 134:207638
TITLE: Synthesis and biological evaluation of 12,13-cyclopropyl and 12,13-cyclobutyl epothilones
AUTHOR(S): Nicolaou, K. C.; Namoto, Kenji; Li, Jim; Ritzen, Andreas; Ulven, Trond; Shoji, Mitsuru; Zaharevitz, Dan; Gussio, Rick; Sackett, Dan L.; Ward, Rita D.; Hensler, Anne; Fojo, Tito; Giannakakou, Paraskevi
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: ChemBioChem (2001), 2(1), 69-75
Published in: Angew. Chem., Int. Ed., 40(1)
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:207638
GI

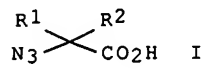


I

AB The authors have constructed two 12,13-cyclopropyl (15S and 15R) and two 12,13-cyclobutyl (15S and 15R) epothilone analogs (e.g. I) by total synthesis and evaluated their biol. activities. While the 15S compds. exhibited potent tubulin polymerization activity and cytotoxicity against tumor cells, the 15R isomers were devoid of such actions. This re-enhanced the view that while the oxygen atom at the C12-C13 site is not necessary for biol. activity, the proper configuration at C15 is absolutely essential for it.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 34 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:30050 HCAPLUS Full-text
DOCUMENT NUMBER: 134:222998
TITLE: α-Azido acids for direct use in solid-phase peptide synthesis
AUTHOR(S): Tornoe, Christian W.; Davis, Peg; Porreca, Frank; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Copenhagen, DK-2500, Den.
SOURCE: Journal of Peptide Science (2000), 6(12), 594-602
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:222998
GI



I

AB Several new α-azido acids, e. g., I [R1, R2 = Me; R1 = Me, R2 = Et; R1, R2 = Et; R1, R2 = Ph; R1 = H, R2 = (CH2)13Me, etc.] have been synthesized and their use in solid-phase peptide synthesis has been demonstrated. The azido group allows for high activation of the carboxyl group as an acid chloride without formation of byproducts and with no detectable racemization. An analog of Leu-enkephalin has been prepared and tested in the mouse vas deferens and guinea pig ileum bioassays: it displays moderate activity at the δ-opioid receptor.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 35 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:845884 HCAPLUS Full-text
DOCUMENT NUMBER: 134:147962
TITLE: Chiral, polyionic dendrimers with complementary

charges - synthesis and chiroptical properties
AUTHOR(S): Ritzen, Andreas; Frejd, Torbjorn
CORPORATE SOURCE: Organic Chemistry 1, Department of Chemistry, Lund University, Lund, 22100, Swed.
SOURCE: European Journal of Organic Chemistry (2000), (22), 3771-3782
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chiral dendrimers up to the second generation have been prepared from enantiopure aromatic bis- and tris(amino acids) by peptide coupling techniques. The dendrimers could be deprotected to yield water-soluble polyamine and/or polycarboxylic acid macromols. Two complementary types, with respect to the charges carried in water at pH = 7, were synthesized. A chiroptical study of the protected dendrimers, which were soluble in THF and CHCl3, was conducted. The results of that study indicate that the solution shapes of these dendrimers are rather decongested, with little steric interaction between different parts of the dendritic structure.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 36 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:780078 HCAPLUS Full-text
DOCUMENT NUMBER: 135:273193
TITLE: Solid-phase synthesis of chemotactic peptides using α-azido acids. [Erratum to document cited in CA133:267143]
AUTHOR(S): Tornoe, Christian W.; Sengelov, Henrik; Meidal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Copenhagen, DK-2500, Den.
SOURCE: Journal of Peptide Science (2000), 6(10), 539
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The corrected Table 1 is given.

L20 ANSWER 37 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:557699 HCAPLUS Full-text
DOCUMENT NUMBER: 133:267143
TITLE: Solid-phase synthesis of chemotactic peptides using α-azido acids
AUTHOR(S): Tornoe, Christian W.; Sengelov, Henrik; Meldal, Morten
CORPORATE SOURCE: Department of Chemistry, Carlsberg Laboratory, Copenhagen, DK-2500, Den.
SOURCE: Journal of Peptide Science (2000), 6(7), 314-320
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:267143
AB Four chemotactic peptides, For-Met-Xxx-Phe-OMe (Xxx = Aib, Deg, Dpg, or Dph, where Aib = 2-aminoisobutyric acid, Deg = diethylglycine, Dpg = dipropylglycine, Dpg = diphenylglycine) with an α,α- disubstituted amino acid at position 2 have been synthesized by the azido acid method on solid-phase,

and were tested for biol. activity. Dpg in the central position was found to be as active as the natural chemotactic peptide for chemotactic activity toward human neutrophils. Higher yields were obtained than previously reported solution-phase syntheses of chemotactic peptides, and EEDQ (2-ethoxy-1-ethoxycarbonyl-1,2- dihydroquinoline) was used successfully for the difficult solid-phase formylation of amino groups.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 38 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:401811 HCAPLUS Full-text

DOCUMENT NUMBER: 133:43427

TITLE: Preparation of benzofurans as 5-HT1A receptor ligands

INVENTOR(S): Andersen, Kim; Rottlander, Mario; Bogeso, Klaus Peter; Pedersen, Henrik; Ruhland, Thomas; Dancer, Robert

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000034263	A1	20000615	WO 1999-DK676		19991203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2353618	A1	20000615	CA 1999-2353618		19991203
BR 9916873	A	20010821	BR 1999-16873		19991203
EP 1137644	A1	20011004	EP 1999-957263		19991203
EP 1137644	B1	20030910			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200101605	T2	20011022	TR 2001-200101605		19991203
HU 200104510	A2	20020429	HU 2001-4510		19991203
JP 2002531556	T	20020924	JP 2000-586710		19991203
AU 759248	B2	20030410	AU 2000-15036		19991203
AT 249451	T	20030915	AT 1999-957263		19991203
NZ 511751	A	20030926	NZ 1999-511751		19991203
PT 1137644	T	20040130	PT 1999-957263		19991203
ES 2204175	T3	20040416	ES 1999-957263		19991203
IL 143082	A	20040620	IL 1999-143082		19991203
ZA 2001003987	A	20020516	ZA 2001-3987		20010516
HR 2001000418	A1	20020630	HR 2001-418		20010601
IN 2001CN00769	A	20050304	IN 2001-CN769		20010601
US 2002032205	A1	20020314	US 2001-874392		20010604
NO 2001002802	A	20010807	NO 2001-2802		20010607
BG 105646	A	20020228	BG 2001-105646		20010625
HK 1043121	A1	20051216	HK 2002-104563		20020619
PRIORITY APPLN. INFO.:			US 1998-111360P	P	19981208
			DK 1998-1631	A	19981209
			WO 1999-DK676	W	19991203

US 2000-632117 A 20000803
WO 2001-US23487 A 20010726

OTHER SOURCE(S): MARPAT 133:43427
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = H, halo, CF3, etc.; R2, R3 = H, CF3, alkyl, etc.; n = 1-5; m = 0-1; A = N(R4)DsZq, II-IV (wherein Z = O, S; s = 0-1; q = 0-1; R4 = H, alkyl, alkenyl, etc.; D = alkylene, alkenylene, alkynylene); B = (un)substituted Ph, indolyl, etc.; Ar = (un)substituted Ph, thienyl, furanyl, etc.] and their pharmaceutically acceptable acid addition salts which are potently binding to the 5-HT1A receptor, were prepared Thus, reacting 5-(4-bromobutyl)-1,4-benzodioxane (preparation given) with (+)-1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran- 5-carbonitrile in the presence of K2CO3 in Me iso-Bu ketone afforded 73% (+)-V which showed IC50 of 39 nM against 3H-5-CT binding and IC50 of 60 nM against serotonin reuptake.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 39 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:290435 HCAPLUS Full-text
DOCUMENT NUMBER: 133:73775
TITLE: Enzymic and chiral HPLC resolution of α-azido acids and amides
AUTHOR(S): Tornoe, Christian W.; Sonke, Theo; Maes, Ilse; Schoemaker, Hans E.; Meldal, Morten
CORPORATE SOURCE: Carlsberg Laboratory, Department of Chemistry, Valby, DK-2500, Den.
SOURCE: Tetrahedron: Asymmetry (2000), 11(5), 1239-1248
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For the first time, enzymic resolution of α-azido acid amides has been successfully demonstrated with high yields and enantiomeric excess. In one case dynamic kinetic resolution was achieved leading to >50% yield of the enantiomerically pure azido acid. Chiral HPLC was also used to sep. racemic α-azido acids, and the separation process was automated. Two routes to enantiopure α-azido acid building blocks for solid-phase peptide synthesis have, therefore, been established.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 40 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:186196 HCAPLUS Full-text
DOCUMENT NUMBER: 132:321523
TITLE: New polyfunctional magnesium reagents for organic synthesis
AUTHOR(S): Rottlander, Mario; Boymond, Laure; Berillon, Laurent; Lepretre, Anne; Varchi, Greta; Avolio, Salvatore; Laaziri, Hamid; Queguiner, Guy; Ricci, Alfredo; Cahiez, Gerard; Knochel, Paul
CORPORATE SOURCE: Institut fur Organische Chemie der Universitat, Munchen, 81377, Germany

SOURCE: Chemistry--A European Journal (2000), 6(5), 767-770
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 20 refs. The iodine-magnesium exchange reaction allows the preparation of polyfunctional aryl, heteroaryl, or alkenyl magnesium reagents at low temperature These reagents display the typical reactivity of Grignard compds. and undergo various copper-catalyzed reactions such as allylation or 1,4-addition Using this halogen-metal exchange reaction, it was possible to generate polyfunctional magnesium reagents on the solid phase.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 41 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:44865 HCAPLUS Full-text
DOCUMENT NUMBER: 132:265469
TITLE: Azido acids in a novel method of solid phase synthesis
AUTHOR(S): Meldal, Morten; Tornoe, Christian; Tedebark, Ulf; Jansson, Anita M.; Juliano, Maria A.; Panza, Luigi; Lay, Luigi
CORPORATE SOURCE: Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemical Diversity, Collected Papers, International Symposium, 5th, London, Sept. 2-6, 1997 (1999), Meeting Date 1997, 19-22. Editor(s): Epton, Roger. Mayflower Scientific Ltd.: Kingswinford, UK.
CODEN: 68OEAA
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium on the authors' work using α-azido amino acids as versatile reagents for solid phase peptide synthesis.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 42 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:659392 HCAPLUS Full-text
DOCUMENT NUMBER: 131:257694
TITLE: Method for the production of Grignard reagents
INVENTOR(S): Boymond, Laure; Rottlander, Mario; Cahiez, Gerard; Knochel, Paul
PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951609	A1	19991014	WO 1999-EP2275	19990401
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19815078	A1	19991007	DE 1998-19815078	19980406
DE 19816414	A1	19991021	DE 1998-19816414	19980414
DE 19836408	A1	20000224	DE 1998-19836408	19980812

CA 2326751	A1	19991014	CA 1999-2326751		19990401
EP 1070070	A1	20010124	EP 1999-914565		19990401
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE					
JP 2003517433	T	20030527	JP 2000-542330		19990401
US 6899830	B1	20050531	US 2000-647069		19990401
PRIORITY APPLN. INFO.:			DE 1998-19815078	A	19980406
			DE 1998-19816414	A	19980414
			DE 1998-19836408	A	19980812
			WO 1999-EP2275	W	19990401

OTHER SOURCE(S): MARPAT 131:257694

AB Grignard reactions of IC6H4R (R = p-Me3CO2C, p-, m-NC, p-EtO2C, p-Br) with BzH gave 89-94% PhCH(OH)C6H4R. Similarly, IC6H4R (R = p-piperidinocarbonyl, p-, o-NC, o-, p-Br) and allyl bromide gave 75-89% H2C:CHCH2C6H4R. Grignard reactions were also carried out supported on Wang resin to give 11 products such as p-RC6H4CO2H (R = allyl, PHCH(OH), NC, PhS), 5-allylthiophene-2-carboxylic acid, 5-cyanofuran-2-carboxylic acid, etc.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 43 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:45319 HCAPLUS Full-text

DOCUMENT NUMBER: 130:252737

TITLE: Synthesis of a chiral dendrimer based on polyfunctional amino acids

AUTHOR(S): Ritzen, Andreas; Frejd, Torbjorn

CORPORATE SOURCE: Department of Chemistry, Organic Chemistry 1, Lund University, Lund, 221 00, Swed.

SOURCE: Chemical Communications (Cambridge) (1999), (2), 207-208
CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A chiral, nonracemic dendrimer of generation two based on nine units of an aromatic bis-amino acid and one unit of protected tris-alanine was obtained through convergent synthesis.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 44 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:773073 HCAPLUS Full-text

DOCUMENT NUMBER: 130:95806

TITLE: Phenyltrisalanine: a new, C3-symmetric, trifunctional amino acid

AUTHOR(S): Ritzen, Andreas; Basu, Basudeb; Wallberg, Andreas; Frejd, Torbjorn

CORPORATE SOURCE: Organic Chemistry 1, Department of Chemistry, Lund University, Lund, SE-221 00, Swed.

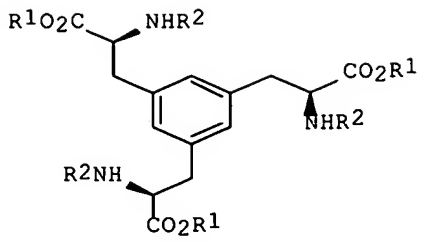
SOURCE: Tetrahedron: Asymmetry (1998), 9(19), 3491-3496
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Two phenyltrisalanine derivs. I (R1 = Me, R2 = Cbz; R1 = CH2Ph, R2 = Boc), new trifunctional amino acids, were synthesized in optically active forms. Two complementary techniques, Horner-Wadsworth-Emmons olefination reaction or Heck coupling reaction, were employed, and the resulting dehydroamino acids were hydrogenated using a chiral Rh(I)-Et-DuPHOS catalyst. Phenyltrisalanine derivs. I were obtained with excellent stereoisomeric purity.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 45 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:631200 HCAPLUS Full-text

DOCUMENT NUMBER: 130:81825

TITLE: Cyclization of meta-phenylene-bis-alanine derivatives

AUTHOR(S): Ritzen, Andreas; Frejd, Torbjorn

CORPORATE SOURCE: Department of Chemistry, Organic Chemistry 1, Lund University, Lund, SE-221 00, Swed.

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1998), (20), 3419-3424
CODEN: JCPRB4; ISSN: 0300-922X

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:81825

AB The cyclization of a meta-phenylene-bis-alanine derivative with several different spacer moieties was investigated. A large difference in the ease of cyclization was observed depending on which path of cyclization was chosen. NMR studies indicate that the closed-loop mols. adopt folded conformations with the loop directly above the aromatic ring plane.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 46 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:467767 HCAPLUS Full-text

DOCUMENT NUMBER: 129:202524

TITLE: Preparation of highly functionalized Grignard reagents by an iodine-magnesium exchange reaction and its application in solid-phase synthesis

AUTHOR(S): Boymond, Laure; Rottlander, Mario; Cahiez, Gerard; Knochel, Paul

CORPORATE SOURCE: Fachbereich Chemie Universitat, Marburg, D-35032, Germany

SOURCE: Angewandte Chemie, International Edition (1998), 37(12), 1701-1703
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

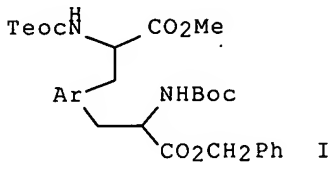
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:202524

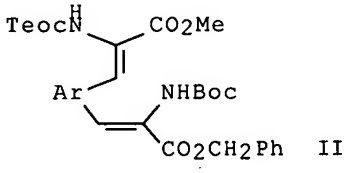
AB Grignard reagents were prepared via iodine-magnesium exchange and the use of the reagents thus obtained was reported. Wang resin was charged with 4-iodobenzoic acid and the mixture was subsequently treated with isopropylmagnesium bromide to give a Grignard reagent. Quenching of the latter with tosyl cyanide gave 4-cyanobenzoic acid, following removal of the resin support.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 47 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:171987 HCAPLUS Full-text
DOCUMENT NUMBER: 128:244304
TITLE: Synthesis of optically active arylene bis-alanine derivatives carrying orthogonal protecting groups
AUTHOR(S): Ritzen, Andreas; Basu, Basudeb; Chattopadhyay, Shital K.; Dossa, Fahreen; Frejd, Torbjorn
CORPORATE SOURCE: Department of Chemistry, Organic Chemistry 1, Lund University, Lund, SE-221 00, Swed.
SOURCE: Tetrahedron: Asymmetry (1998), 9(3), 503-512
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:244304
GI



I



II

AB Derivs. of p- and m-phenylene bis-alanine and related biphenyl systems I [Ar = p-C6H4, m-C6H4, p,p'-(C6H4)2; Teoc = Me3SiCH2CH2O2C; Boc = Me3CO2C], carrying four orthogonal protecting groups, were synthesized via combinations of Heck couplings of haloarenes and dehydroalanine derivs. followed by asym. hydrogenations. The intermediate unsatd. arylalanine derivs. II were hydrogenated using [Rh(COD)((R,R)-DIPAMP)]+BF4- or [Rh(COD)(Me-DuPHOS)]+X- as catalysts to produce the optically active, protected amino acid derivs. in ≥98% e.e. as analyzed by chiral phase HPLC.

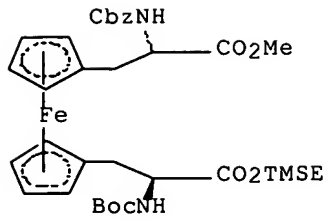
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 48 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:643210 HCAPLUS Full-text
DOCUMENT NUMBER: 127:358692
TITLE: Multiple cross-coupling reactions of aryl and benzylic zinc halides with aryl halides and triflates in solid-phase synthesis of polyfunctional aromatics
AUTHOR(S): Rottlander, Mario; Knochel, Paul
CORPORATE SOURCE: Fachbereich Chemie, Philipps-Universitat, Marburg,

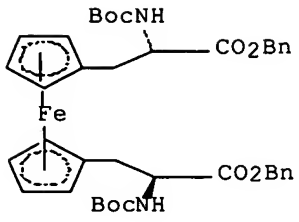
D-35032, Germany
SOURCE: Synlett (1997), (9), 1084-1086
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:358692
AB Aryl and benzylic zinc bromides undergo efficient Pd(0)-catalyzed cross-coupling reactions on the solid-phase using either Rink or Wang resin. By performing the cross-couplings with the multi-coupling reagents 4-BrZnCH2C6H4O2CCF3 and 4-BrZnC6H4OSi(CHMe2)3, two successive C-C bond forming reactions are possible on the solid-phase.

L20 ANSWER 49 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:480607 HCAPLUS Full-text
DOCUMENT NUMBER: 127:161856
TITLE: New coupling reactions and phosphorylations using organozinc reagents
AUTHOR(S): Knochel, Paul; Langer, Falk; Longeau, Alexia; Rottlander, Mario; Studemann, Thomas
CORPORATE SOURCE: Fachbereich Chemie, Philipps-Universitat, Marburg, D-35032, Germany
SOURCE: Chemische Berichte/Recueil (1997), 130(8), 1021-1027
CODEN: CHBRFW
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 42 refs. This microreview on the chemical of organozinc reagents starts by briefly showing the methods of preparation of organozinc compds. and then discusses the considerable synthetic utility of zinc organometallics for the formation of new carbon-carbon bonds in the presence of transition-metal catalysts. Finally, the use of organozinc chemical for the preparation of polyfunctional and chiral phosphines is described.

L20 ANSWER 50 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:419565 HCAPLUS Full-text
DOCUMENT NUMBER: 127:176531
TITLE: Synthesis of optically active 1,1'-ferrocenylenebis(alanine) carrying four different protecting groups
AUTHOR(S): Basu, Basudeb; Chattopadhyay, Shital K.; Ritzen, Andreas; Frejd, Torbjoern
CORPORATE SOURCE: Division of Organic Chemistry 1, Department of Chemistry, Lund University, Lund, S-221 00, Swed.
SOURCE: Tetrahedron: Asymmetry (1997), 8(11), 1841-1846
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:176531
GI



I



II

AB The bis-amino acid derivs. (+)-6 and (+)-8 (shown as I and II, resp. where TMSE = 2-trimethylsilylethyl and Bn = benzyl) were synthesized (>95% ee) as mixts. with the corresponding diastereomers (dr:s 80:20 and 90:10, resp.) via asym. hydrogenation of the corresponding bis(didehydroamino acid) derivs. using [Rh((R,R)-DIPAMP)(COD)]BF4 (DIPAMP = 1,2-bis[(o-methoxyphenyl)phenylphosphino]ethane) as catalyst.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 51 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:424819 HCAPLUS Full-text
DOCUMENT NUMBER: 119:24819
TITLE: Acetylcholine receptor molecules of the nematode Caenorhabditis elegans
AUTHOR(S): Fleming, J. T.; Tornoe, C.; Riina, H. A.; Coadwell, J.; Lewis, J. A.; Sattelle, D. B.
CORPORATE SOURCE: Lab. Mol. Signalling, AFRC, Cambridge, CB2 3EJ, UK
SOURCE: EXS (1993), 63(Comparative Molecular Neurobiology), 65-80
CODEN: EXSEE7; ISSN: 1023-294X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 49 refs. Studies using physiol. and biochem. methods have revealed the existence of nicotinic acetylcholine receptors with a novel pharmacol. C. elegans provides a particularly suitable organism with which to investigate such receptors using mol. genetic approaches.

L20 ANSWER 52 OF 52 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:404456 HCAPLUS Full-text
DOCUMENT NUMBER: 109:4456
TITLE: Lipoprotein-bound bile acids in serum from healthy men, postprandially and during fasting
AUTHOR(S): Hedenborg, G.; Norman, A.; Ritzen, A.
CORPORATE SOURCE: Dep. Clin. Chem., Karolinska Sjukhuset, Stockholm, 104 01, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1988), 48(3), 241-5
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Individual bile acids were determined by gas-liquid chromatog. in very-low-d., low-d., and hi-d. lipoprotein fractions obtained by sequential ultracentrifugation of serum from normal adults, both postprandially and during fasting (for ≥12 h). The lipoproteins contained 22-34% of fasting serum bile acids. The observed postprandial increase in bile acids did not exhibit any shift in the ratio between lipoprotein-bound- and non-lipoprotein-bound bile acids. Bile acids were present in all isolated lipoprotein

fractions, with high-d. lipoproteins containing the highest amts. In the lipoprotein fraction, a higher percentage of cholate than of chenodeoxycholate was found.

=>